

Comparison of Articaine and Prilocaine Anesthesia by Infiltration in Maxillary and Mandibular Arches

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Claims that labial infiltration of the local anesthetic articaine HCl (Ultracaine DS™) results in anesthesia of mandibular pulpal as well as maxillary and mandibular lingual soft tissue have never been scientifically substantiated. The aim of this investigation was to evaluate these claims, by comparing articaine to a standard anesthetic, prilocaine HCl (Citanest Forte™). To investigate this, a double blind, randomized study was conducted in healthy adult volunteers. In each volunteer, the ability to induce maxillary and mandibular anesthesia following labial infiltration with articaine was compared to prilocaine given contralaterally. Anesthesia was determined by measuring sensation to electrical stimulation at the tooth, labial and lingual soft tissue for each of the 4 non-carious, non-restored, canines.

Results showed that mandibular canine pulpal anesthesia had a success rate of 65% for articaine and 50% for prilocaine. Success rates for palatal and lingual anesthesia averaged 5% for each agent. As determined by chi-square analysis, no statistically significant differences were found between articaine and prilocaine for any tissue at any of the 6 sites ($P > 0.05$). A time-course assessment also failed to demonstrate a difference between the two drugs. Therefore these data are not consistent with superior anesthesia efficacy being produced by articaine at any site, including the mandibular pulpal, lingual or maxillary palatal tissues, in the canine teeth studied.

It is commonly accepted that in order to achieve local anesthesia for procedures on teeth or buccal soft tissue in the maxillary arch, administration of local anesthetics by buccal infiltration, also known as a paraperiosteal field block, is routinely successful. Palatal soft tissue anesthesia requires a separate palatal injection, a technique that is often painful for the patient. Any local anesthetic that would permit use of buccal infiltration to gain palatal anesthesia would be of great advantage in dentistry. For procedures in the mandibular arch, in adults, the thickness of buccal cortical bone precludes buccal infiltration approaches producing pulpal or lingual soft tissue anesthesia, necessitating administration of local anesthetic by nerve block techniques. The use of nerve blocks has several disadvantages compared with the infiltration technique. One drawback is the greater failure rate which is reported at approximately 15%,¹ and any reduction in that rate would be a welcome improvement for dentists and their patients. A second disadvantage is the greater incidence of complications such as trismus, hematoma or paresthesia associated with nerve block as compared to infiltration.¹ A third drawback is the requirement of anesthetizing the entire branch of the inferior alveolar nerve, even if only one tooth is being treated. For certain patients, the lack of the anesthetized sensation of the lower lip would be preferable. Again, therefore, any local anesthetic that would permit use of infiltration in the mandible would be of great value in dentistry.

The relatively new local anesthetic articaine HCl (Ultracaine) has been claimed to be efficacious for anesthesia of mandibular pulpal and lingual soft tissue by labial (buccal) infiltration, as well as palatal soft tissue anesthesia by means of maxillary labial infiltration. This would be of important clinical benefit as it is in contrast to commonly-used anesthetics which are efficacious by infiltration for labial soft tissue and maxillary pulpal anesthesia only. Since its introduction in Canada in 1983, articaine has achieved wide use in dentistry, primarily based on the belief of these superior properties. However, a review of the literature²⁻²⁰ fails to reveal any scientific study demonstrating this. The aim of this investigation was to verify these claims, by comparing articaine to a commonly-used

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Table 1. Inclusion and Exclusion Criteria

Inclusion: All volunteers had to satisfy the following to be included in the study:

1. Between 18 to 50 years of age
2. In good medical health.
3. Teeth 13, 23, 33, 43 present in satisfactory condition with no restorations
4. Must give informed written consent prior to participation.

Exclusion Criteria: Subjects with any of the following were excluded from the study:

1. Allergies to amide local anesthetics or any of the ingredients in the cartridges.
2. Pregnant females.
3. History of any significant medical conditions.
4. Taking any medications which may influence the anesthetic assesment, such as analgesics, anti-inflammatories or sedative drugs.
5. Active oral or dental pathology or undergoing treatment at the tested sites.
6. Presence of restorative dental work at the tested sites.
7. Inability to provide informed consent.

local anesthetic, prilocaine HCl (Citanest Forte). Citanest Forte is an appropriate control as it is among the most commonly used local anesthetics in dentistry and both of these formulations have the same concentration of epinephrine (1 : 200,000).

Therefore a double-blind randomized trial was designed to test the null hypothesis that articaine was equivalent to prilocaine with respect to the ability to induce pulpal and lingual anesthesia when administered by labial infiltration. The primary objective was to determine if anesthesia was successful. In addition, it was an aim of this study to characterize the time course response of each drug, and to collect data on the ability to induce mandibular pulpal anesthesia in adults by labial infiltration of local anesthetics.

METHODS

Subjects of either sex were screened as to their medical health and the health of the canine teeth, with only non-carious, non-restored teeth used. Inclusion and exclusion criteria for this study are listed in Table 1. The average age of the subjects was 25 years (range of 22 to 32). This protocol was approved the Human Ethics Committee of the University of Toronto.

The two drugs being compared were 4% prilocaine with epinephrine 1 : 200,000 (Citanest Forte) and 4% articaine with epinephrine 1 : 200,000 (Ultracaine DS). Self-aspirating syringes were used, calibrated and marked on the shank to indicate where 1.5 ml would be administered. The cartridges were covered with an adhesive paper label, leaving only a 4 mm window adjacent to the cap to allow

visualization of the aspiration results, yet concealing the type of anesthetic. The cartridge was loaded by a nurse assistant so that neither the subject nor the dentist administering the anesthetic was aware of which preparation was being injected.

This study was double blind, with the order of drug administration randomized. A standard paraperiosteal field block ("infiltration") was given to each of teeth #13, 23, 33 and 43. If prilocaine was selected for administration to tooth 13, articaine was subsequently administered to tooth 23. Similarly, one anesthetic was then randomly selected for tooth 33, followed by administration of the other anesthetic to tooth 43. The injection technique was done as usual,¹ with 1.5 ml administered slowly, over a 20 second period. No topical anesthetic was given so as to avoid a potential confounding variable. Routine precautions were taken during the administration of all injections. A new needle was used for each of the four injections. The same syringe was used for each of the four injections on the same subject.

Efficacy of anesthesia was assessed by comparing the ability of each agent to block sensation as determined by electric pulp stimulator (EPS) readings, a method used previously.^{6,19,21} Each tooth had EPS readings (Analytic Technology Corp., Redmond, Washington), in triplicate, at the labial soft tissue, lingual (palatal) soft tissue and on tooth itself. In order to obtain a baseline reading, in the time period from 5 minutes prior to the first injection, the EPS was applied to each of the three tissues and the sweep scale increased until the patient indicated a definite sensation had been felt, and this numerical reading was recorded by the nurse assistant. The sweep range was set initially at 0, with electro-conducting cream (Cardio-Cream, Ingram and Bell, Toronto) used as the interface medium. The electrode was applied to the gingiva 5 mm superior to the gingival margin when maxillary sites were assessed, and 5 mm inferior to the gingival margin when mandibular sites were being assessed. The electrode was applied to the labial midportion of the tooth when assessing pulpal responses. Three recordings were made at each site and then the median value used for data analysis. This median value, and not the average, was used in order to eliminate the potential skewing of data due to improper placement of probe that could have resulted in an extreme value.

Injection occurred at time "0." Beginning at 1 minute and ending by 5 minutes (therefore midpoint of 3 minutes) post-injection, this same sequence of EPS testing at each of the 3 sites, in triplicate, was repeated. Again, beginning at 6 minutes the above protocol was repeated and continued until 25 minutes post-injection. Thus, the median time point for each triplicate assessment was -3, +3, +8, +13, +18 and +23 minutes. If no sensation was felt by the maximal level, this reading was recorded ("80").

Whenever sensation was felt on the palatal soft tissue (EPS reading of less than 80), the tissue at the palatal gingival margin of the tooth in question was probed with a periodontal probe to rule out involvement of the nasopalatine nerve and the subject asked if a sensation could be felt. Either a "yes" or "no" response was recorded, and any discrepancy between electrical and tactile responses reported as such.

Therefore, there was a recording of EPS measurements made in triplicate for 6 time points at each of 3 sites at each of 4 canines. Successful anesthesia was defined as a median value of 80, which is the maximal EPS reading possible, for any triplicate recording at any one of the post-injection time-points.

The parallel study in the posterior arches²² was identical to that described above, except that second molars were used instead of canines.

Statistical Analysis:

The data collected were of 2 types: success of anesthesia and time-course response of EPS readings. The primary information was the determination of anesthesia, "yes" or "no." These data were analyzed using the Chi-square test, with $P < 0.05$ judged to be statistically significant. Efficacy of anesthesia of articaine on one maxillary tooth and adjacent soft tissue was compared to prilocaine on the corresponding contralateral tooth and adjacent soft tissue. Similarly, efficacy of anesthesia in the mandibular site was compared to the corresponding contralateral mandibular site. The primary interest was success of pulpal anesthesia in the mandible. The secondary interest was lingual (palatal) soft tissue anesthesia in the mandible and the maxilla.

In addition to the chi-square analysis of success of anesthesia, we also looked at the time course effect on the EPS readings for each anesthetic, at each tissue site. These particular data were analyzed using analysis of variance for repeated measures, and if significance found ($P < 0.05$) this would have been followed by a multiple comparison test, Fisher's Protected Least Significant Difference Test.

Sample Size Calculation:

This was calculated for our major interest, mandibular pulpal anesthesia, based on the following formula^{23,24}:

$$n = \frac{(Z_\alpha + Z_\beta)^2 \times [P_E(1 - P_E) + P_C(1 - P_C)]}{(P_E - P_C)^2}$$

$$= \frac{(1.64 + 1.64)^2 \times [(0.85 \times 0.15) + (0.4 \times 0.6)]}{(0.85 - 0.4)^2}$$

$$= 19.5$$

where n = sample size.

Z_α = normal deviate for alpha. In this case we desired an alpha level of 0.05 and a one sided test as we were only interested in the finding that articaine is more efficacious than prilocaine and not less.

Table 2. Success of anesthesia in mandibular anterior arch.

Tissue	Drug	Yes	No	Success Rate
Pulp:	Prilocaine	10	10	50%
	Articaine	13	7	65%
Lingual tissue:	Prilocaine	1	19	5%
	Articaine	2	18	10%
Labial tissue:	Prilocaine	17	3	85%
	Articaine	17	3	85%

Successful anesthesia was defined as one maximal median EPS value at any one (or more) time point post-injection. For each of the three tissues, no statistically significant differences were found between articaine and prilocaine in the success rates of anesthesia.

Z_β = normal deviate for β . We desired a high Power of 0.95, β level = 0.05. In other words we required a low probability of making a false negative error.

P_E = probability of success for the experimental (articaine) group. Given that the success rate for mandibular block anesthesia is 0.85,¹ we needed a level at least as good as 0.85.

P_C = probability of success for the control (prilocaine) group. Little data are available for this, but we estimated a value of 0.40.

Therefore a sample size of 20 was required for each treatment and control group, and given that the patient is his/her own control, the final sample size remained 20.

RESULTS

The results of the experiment on canines are shown in Figures 1-6 and Tables 2 and 3. The primary interest was success of anesthesia in the mandibular pulp. As shown in Table 2, articaine induced mandibular canine pulpal anesthesia in 65% of the subjects tested compared to 50% for prilocaine. This is not a statistically significant difference as determined by the chi-square analysis. The time course of mandibular pulpal anesthesia is shown in Figure 1. It can be seen that there was no difference between the two drugs in the pattern of loss of sensation. This was confirmed by the analysis of variance for repeated measures which showed no statistically significant differences between articaine and prilocaine. Maximal anesthesia peaked at 8 minutes post-administration, and then a plateau was evident for the remaining time-points assessed.

The success rate for mandibular lingual anesthesia is shown in Table 2. Articaine induced anesthesia in 10% of the subjects compared to 5% for prilocaine. This is not a statistically significant difference as determined by the chi-square analysis. The time course of lingual anesthesia is shown in Figure 2, where it can be seen that there was

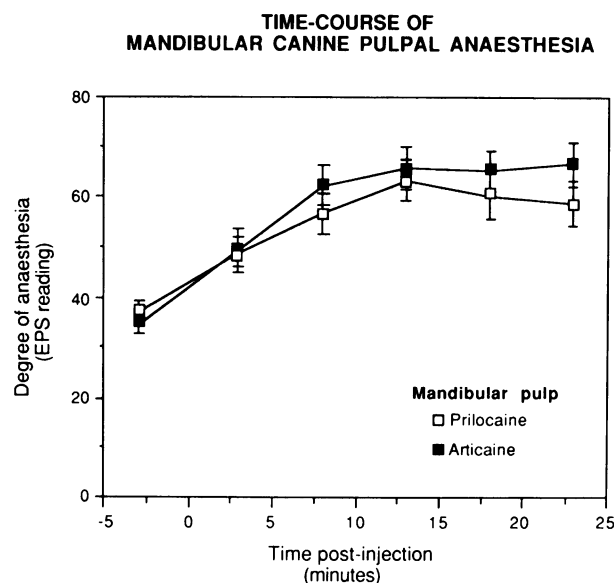


Figure 1. The time-course of mandibular canine pulpal anesthesia is shown above. EPS values are the mean \pm the standard error of the mean (SEM) of the median values for each of the 20 subjects at the 6 time-points assessed. Injection took place at time "0." No statistically significant differences between articaine and prilocaine were found.

no difference between the two drugs in the pattern of anesthesia. There was a minimal loss of sensation noted, with the peak occurring at 8 minutes post-administration, and not changing subsequently.

The control for the mandibular arch was labial soft tissue anesthesia, and Table 2 shows that anesthesia was induced in 85% of the subjects for both articaine and prilocaine. Figure 3 shows the time-course effect characterized by a prompt onset of anesthesia, maximal loss of sensation noted at 8 minutes post-injection, with no change subsequently. Again, no significant difference was detected between the two anesthetics.

The results for anesthesia in the maxillary arch are listed in Table 3. The primary site of interest here was the palate. It can be seen that articaine did not induce anesthesia (0%) in any patients at all, whereas prilocaine had a 5% success rate. This difference is not statistically significant. The time-course response is shown in Figure 4, which illustrates no difference between the agents, and only a marginal loss of sensation detected post-administration. The results of tactile stimulation confirmed the EPS testing with 2 exceptions. Tactile sensation was lost with two articaine administrations, implying that anesthesia could have been successful, and the positive EPS reading due to conduction by the nasopalatine nerve from a more proximal site. This discrepancy with the EPS reading does not affect the lack of statistical significance between the two drugs.

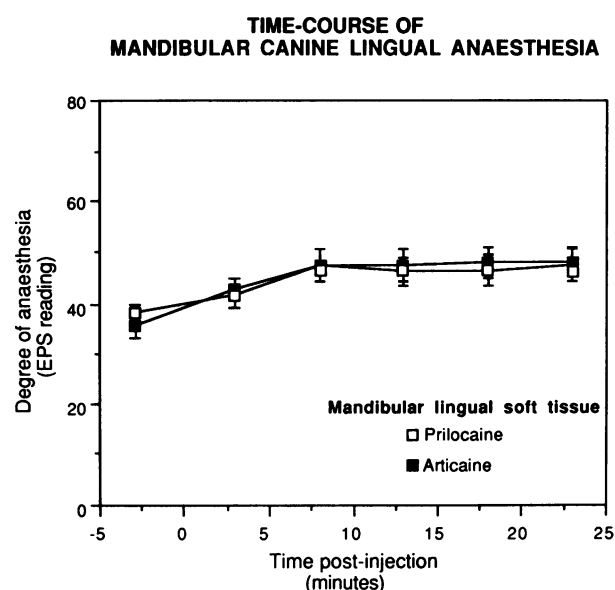


Figure 2. The time-course of mandibular lingual anesthesia is shown above. EPS values are the mean \pm SEM of the median values for each of the 20 subjects. No statistically significant differences between articaine and prilocaine were found.

The controls for the maxillary arch are the pulpal and labial tissues. Table 3 lists the success rates for pulpal anesthesia which were 65% for each agent. The time course is shown in Figure 5, and it can be seen that maximal anesthesia was reached by 8 minutes post-injection, with no change noted subsequently. Again no statisti-

Figure 3. The time-course of mandibular labial anesthesia is shown above. EPS values are the mean \pm SEM of the median values for each of the 20 subjects. No statistically significant differences between articaine and prilocaine were found.

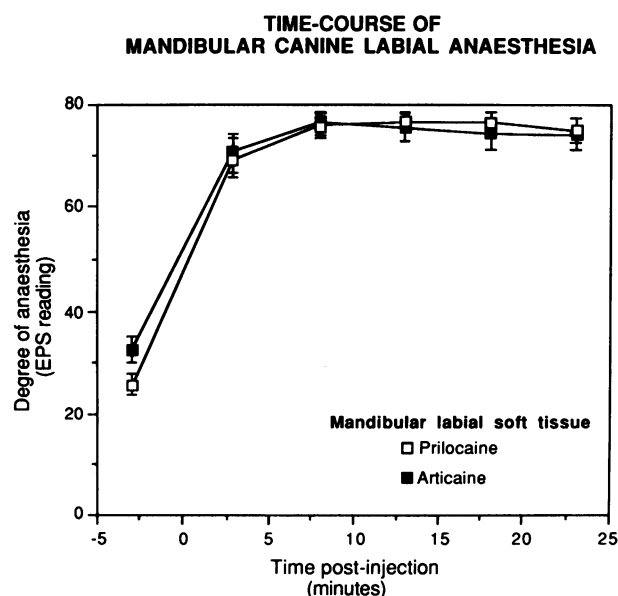


Table 3. Success of anesthesia in maxillary anterior arch.

Tissue	Drug	Yes	No	Success Rate
Pulp:	Prilocaine	13	7	65%
	Articaine	13	7	65%
Palatal tissue:	Prilocaine	1	19	5%
	Articaine	0	20	0%
Labial tissue:	Prilocaine	16	4	80%
	Articaine	18	2	90%

For each of the three tissues, no statistically significant differences were found between articaine and prilocaine in the success rates of anesthesia.

cal difference between articaine and prilocaine was detected.

As stated in Table 3, anesthesia in labial soft tissue was induced in 90% of the subjects with articaine compared with 80% success for prilocaine. This difference is not statistically significant. Once again, as shown in Figure 6, the time-course of anesthesia shows that both drugs had a rapid onset, with peak loss of sensation found at 8 minutes post-administration, with a plateau effect noted thereafter.

DISCUSSION

The data presented are not consistent with the putative ability of articaine to induce anesthesia of mandibular pulp, lingual tissue or maxillary palatal tissue, when ad-

Figure 4. The time-course of maxillary palatal anesthesia is shown above. EPS values are the mean \pm SEM of the median values for each of the 20 subjects. No statistically significant differences between articaine and prilocaine were found.

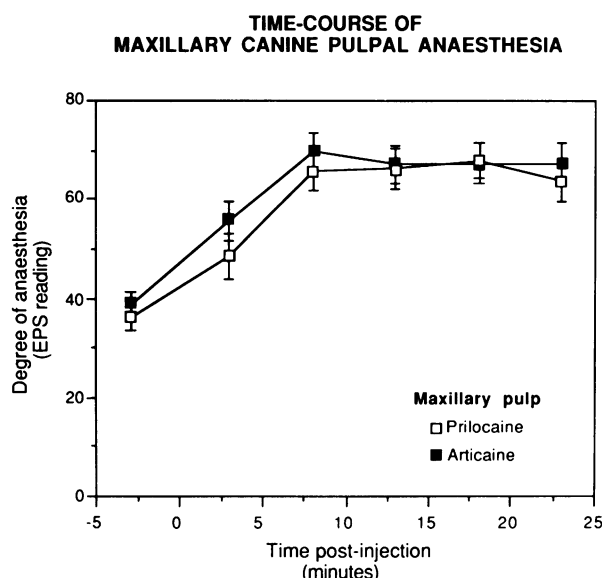
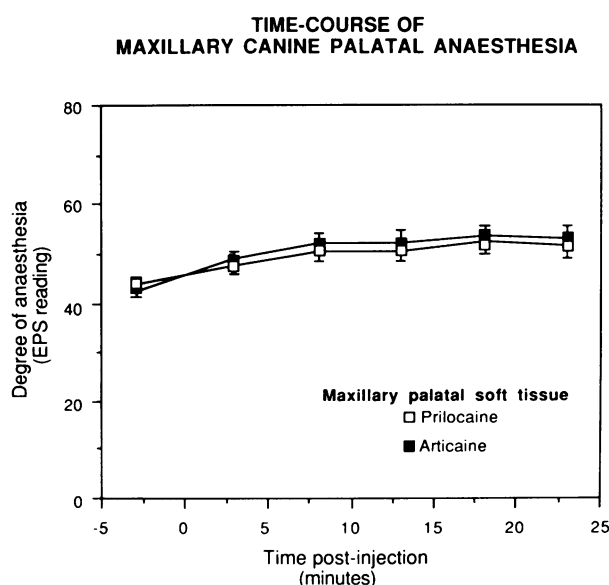


Figure 5. The time-course of maxillary canine pulp anesthesia is shown above. EPS values are the mean \pm SEM of the median values for each of the 20 subjects. No statistically significant differences between articaine and prilocaine were found.

ministered by labial infiltration. No statistically significant differences were detected whether anesthesia was assessed by absolute determinants (yes or no) or over a time-course for up to 25 minutes post-administration. This study is unique in that it directly tested the hypothesis that

Figure 6. The time-course of maxillary labial anesthesia is shown above. EPS values are the mean \pm SEM of the median values for each of the 20 subjects. No statistically significant differences between articaine and prilocaine were found.

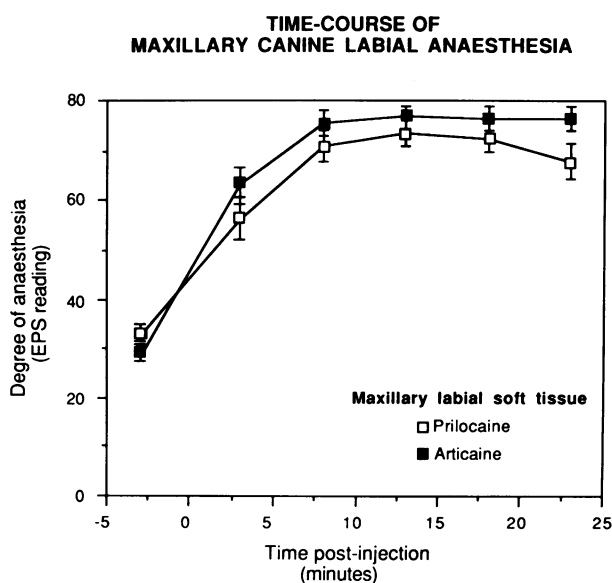


Table 4. Overall success of anesthesia in mandibular posterior and anterior arches.

Tissue	Drug	Yes	No	Success Rate
Pulp:	Prilocaine	20	19	51%
	Articaine	25	14	64%
Lingual tissue:	Prilocaine	8	31	21%
	Articaine	12	28	30%
Buccal tissue:	Prilocaine	35	5	88%
	Articaine	35	5	88%

These data combine the results of the studies on canine and second molars. For each of the three tissues, no statistically significant differences were found between articaine and prilocaine in the success rates of anesthesia. Where $n = 39$, one subject's recordings were rejected due to baseline readings of complete anesthesia.

articaine is equivalent to another commonly-used local anesthetic in its ability to induce mandibular pulpal, lingual or maxillary palatal anesthesia when administered by labial infiltration. The data documented above show that we cannot reject this hypothesis.

Anterior and posterior sites may differ with respect to cortical bone thickness, thereby possibly affecting the success of infiltration approaches. It may be possible that the success of infiltration anesthesia in the canine region could differ compared to the posterior. We have therefore conducted a parallel study in the posterior, using an identical protocol as this study, only substituting second molars for canines.²² The results on second molars were consistent with the canine data in that no statistically significant differences were found. Tables 4 and 5 show the combined data on canines and second molars in both arches. It can be seen that even when combined, the lack of statistically significant differences remain for each of the control or test sites.

Can mandibular infiltration replace mandibular block? This is an important question, since, if true, it would avoid numerous clinical complications as outlined in the Introduction. The data for this are lacking. As shown in Tables 4 and 5, the overall success for anterior and posterior mandibular anesthesia was 64% for articaine compared to 51% for prilocaine, not statistically different for the sample size of 39. Of course, it is possible to gain statistical significance for any magnitude of difference, regardless of how small, provided that the sample size is large enough. The more relevant question however would be, is this difference clinically important, given that the reported success for mandibular block is 85%¹? One needs to test this within the same experimental design to compare the success rates. One possible experiment could directly measure EPS readings of infiltration and compare to block on the contralateral side. Two drawbacks are inherent in this potential experiment. One is the lack of ability to blind

Table 5. Overall success of anesthesia in maxillary posterior and anterior arches.

Tissue	Drug	Yes	No	Success Rate
Pulp:	Prilocaine	31	9	78%
	Articaine	32	8	80%
Palatal tissue:	Prilocaine	7	33	18%
	Articaine	8	32	20%
Labial tissue:	Prilocaine	36	4	90%
	Articaine	38	2	95%

These data combine the results of the studies on canine and second molars. For each of the three tissues, no statistically significant differences were found between articaine and prilocaine in the success rates of anesthesia.

such a study. The second is that mandibular block is more susceptible to variation in success dependent on patients' anatomical variation and ability of the clinician administering the block. This second drawback could conceivably be circumvented by selecting a large enough sample size. Therefore, this question remains to be answered, and based on this study, there is no evidence to suspect that one agent is more efficacious for this than another. If our data reflect the true success rate for anesthesia by mandibular infiltration, it may be that pulpal anesthesia will succeed in approximately 60% of the time. That this is clinically satisfactory is unlikely if the 85% success rate proves to be accurate under the same experimental conditions.

Articaine (Ultracaine) has achieved wide use in Canada since its introduction in 1983. The basis for this increasingly common use is the belief that articaine has superior properties with respect to diffusion into tissue, which allows it to induce pulpal and lingual anesthesia in the mandible, and palatal anesthesia in the maxilla, when administered labially. This supposition has found its way into a standard textbook of local anesthesia¹ although it acknowledges that research must be done to verify this claim. A review of the literature on articaine²⁻²⁰ fails to show any scientific study that has assessed the hypothesis that articaine is superior to any other local anesthetic with respect to mandibular pulpal, lingual or palatal anesthesia when administered by labial infiltration. Several studies that have compared articaine to other standard anesthetics such as lidocaine, mepivacaine, prilocaine or procaine, show no significant differences among them, whether tested in vivo^{4-6,8,16} or in vitro.³ One study⁶ compared articaine to prilocaine with respect to maxillary infiltration and mandibular nerve block. This double-blind study demonstrated no statistically significant differences between the two drugs for these two blocks as assessed by the ability to induce anesthesia. Our results with maxillary infiltration confirm these authors' findings. Other studies

have shown articaine as effective in infiltration anesthesia for standard dental injections,^{7,13,20} including the ability of articaine-induced infiltration anesthesia to permit restorative dentistry to be carried out in children. It is commonly accepted that infiltration of any local anesthetic can induce anesthesia in children,¹ therefore it should not be surprising that articaine can do the same. These studies lacked any control as no other anesthetic agent was assessed, therefore comparisons leading to a conclusion of superior efficacy cannot be made.

Unless there is experimental evidence demonstrating superior diffusion capabilities, these claims must be recognized as speculation only. It is important that dentists do not base their use of a drug on speculative, unsubstantiated, claims. This is particularly true of a drug that in many dental offices could be administered numerous times daily, as local anesthetics are. Prudent clinical practice should be based on evidence supported scientifically. Prior to making statements of superior abilities of any drug, one must test this using a scientifically valid approach, such as a randomized, double-blind trial comparing the test drug to a control. Such was the approach of this investigation. This study used a sample size that should have been sufficient to allow for a demonstration of a statistically significant difference if one existed, but this did not occur. As well, articaine was compared to a control drug, with each subject acting as his/her own control.

In conclusion therefore, this controlled, double-blind, randomized trial tested the hypothesis that articaine was equivalent to prilocaine with respect to ability to induce anesthesia of labial, lingual and pulpal tissues, when administered by labial infiltration. In each case we could not reject the hypothesis as no statistically significant differences were found. Therefore, to date, there is no peer-reviewed, scientific, published report of a superior capability of articaine in regard to infiltration anesthesia. Only if these claims of unique properties of articaine are scientifically substantiated should they be made. Otherwise those who make such claims should recognize that it remains as unproven speculation.

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